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**COMMUNICATION FROM THE COMMISSION TO THE EUROPEAN
PARLIAMENT AND THE COUNCIL
ON MEDICAL APPLICATIONS OF IONIZING RADIATION
AND SECURITY OF SUPPLY OF RADIOISOTOPES FOR NUCLEAR MEDICINE**

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1. MAIN EU INSTRUMENTS RELEVANT TO THE MEDICAL APPLICATIONS OF IONIZING RADIATION

1.1. Instruments under Euratom provisions

1.1.1. Legislative tools

The Euratom Basic Safety Standards Directive¹ defines the European legal framework for radiation protection of workers and the general public, based on the following main principles:

- Justification of all new types of practices resulting in exposure to ionizing radiation before being first adopted by their economic, social or other benefits in relation to the health detriment they may cause.
- Optimisation of protection to ensure that the radiation exposures of workers, members of the public and the population as a whole are kept as low as reasonably achievable, economic and social factors being taken into account.
- Limitation of the exposure to ensure that the sum of the radiation doses from all relevant practices will not exceed the legal dose limits for workers or members of the public. Dose limits do not apply to patients and other medically exposed individuals.

The Basic Safety Standards Directive establishes a system of national reporting and regulatory authorization of activities resulting in exposure to ionizing radiation. It also requires a system of inspection to enforce the legal requirements to be established in Member States.

The Medical Exposure Directive² supplements the Basic Safety Standards Directive by providing specific requirements for health protection of patients and other medically exposed individuals against the dangers from ionizing radiation. The Medical Exposure Directive provides a legal framework based on the basic radiation protection principles of justification and optimization taking into account the specificity of medical exposure as deliberate exposure of people for their own health benefit.

The Basic Safety Standards Directive is currently being recast with four other radiation protection Directives, including the Medical Exposure Directive.

1.1.2. Other tools

The Commission acts in multiple other ways to support the safe use of ionizing radiation in medicine, including elaboration of European guidelines, support of research on medical applications of ionizing radiation and involvement in activities fostering information exchange and involvement of stakeholders.

¹ Council Directive 96/29/Euratom of 13 May 1996 laying down basic safety standards for the protection of the health of workers and the general public against the dangers arising from ionizing radiation, OJ L 159, 29 June 1996

² Council Directive 97/43/Euratom of 30 June 1997 on health protection of individuals against the dangers of ionizing radiation in relation to medical exposure, and repealing Directive 84/466/Euratom, OJ L 180, 9 July 1997

The Directorate-General for Energy maintains a Radiation Protection publications series³, which is a useful source of information and guidelines on specific aspects of radiation protection, including on medical exposure. The Commission published in this series studies and guidelines on training of medical staff in radiation protection, referral guidelines for imaging, diagnostic reference levels, acceptability criteria for medical installations, etc. Most recently, guidelines have been published on the evaluation of population doses from medical radiodiagnostic procedures (RP 154) and on clinical audit (RP 159).

Euratom Framework Programme 7 is currently funding a number of projects on medical uses of radiation, the expected impact being an optimisation of doses to patients in clinical practice through improving knowledge and perfecting imaging practices and techniques⁴. Better understanding of the effects of and associated risks from doses of radiation received during medical examinations has been identified as a priority topic by the "High Level Expert Group on Low Dose Risk Research"⁵.

The Joint Research Centre, through the Institute for Transuranium Elements (ITU, Karlsruhe), uses its unique facilities and expertise in handling highly radioactive alpha-emitting nuclides to develop, produce and test novel methods for cancer treatment⁶. In addition ITU is contributing to pre-clinical studies and clinical trials through the provision of radioisotopes, training, equipment and radiochemical support to hospitals and cancer research centres.

The Commission supports information exchange and co-operation between Member States and with stakeholders on issues relating to the use of ionizing radiation in medicine. In 2010 the Commission launched the European Medical ALARA Network (EMAN)⁷ as a stakeholders' network dealing with radiation protection of patients and medical staff. The Commission organizes or co-sponsors ad-hoc meetings on different aspects of the safe use of radiation in medicine⁸ and participates in the activities of regional, European and international networks and organizations.

In its work on radiation protection of patients the Commission is advised by the Working Party on Medical Exposure of the Group of Experts created under Article 31 of the Euratom Treaty⁹. Medical exposure topics are an important part of the annual scientific seminars¹⁰ organized by the Article 31 Group of Experts to review the research implications on the health and safety standards.

1.2. Instruments under EC provisions

1.2.1. Legislative tools

Equipment used in the medical exposure procedures falls under the requirements of Council Directive 93/42/EEC, amended by Directive 2007/47/EC¹¹. The Directive's main purpose is to

³ http://ec.europa.eu/energy/nuclear/radiation_protection/publications_en.htm

⁴ <http://cordis.europa.eu/fp7/euratom>

⁵ <http://www.hleg.de>

⁶ <http://itu.jrc.ec.europa.eu>

⁷ <http://www.eman-network.eu>

⁸ http://ec.europa.eu/energy/nuclear/events/index_en.htm

⁹ http://ec.europa.eu/energy/nuclear/radiation_protection/article_31_en.htm

¹⁰ http://ec.europa.eu/energy/nuclear/radiation_protection/scientific_seminar_en.htm

¹¹ Council Directive 93/42/EEC of 14 June 1993 concerning medical devices, OJ L 169, 12 July 1993; amended by Directive 2007/47/EC of the European Parliament and of the Council of 5 September 2007, OJ L 247, 21 September 2007

ensure that medical devices placed on the European market do not compromise the safety and health of patients, users and other individuals. This legal framework specifies that the emission of unintended radiation must be reduced as far as possible (Article 11.3.1) and that the instructions for use must give sufficiently detailed information in order to avoid the misuses (Article 11.4.1). The medical devices must meet the essential requirements for their design and construction, including those for justification of the intended use of the equipment on the basis of risk/benefit weighting (Article 11.2.1) and for incorporation of technical features for radiation protection of patients, users and other individuals (Articles 11.1.1 and 11.3.1). This is ensured, inter alia, through a system of harmonized standards (Article 5)¹², pre-market conformity assessment procedures (Article 11) and appropriate supervision by the competent authorities (Articles 11.13, 14.1, 14.2, 15.1, 15.2 and 15.7). The Commission is considering a revision of the legal framework for medical devices

According to Council Recommendation on patient safety¹³ patients should be informed of patient safety standards, best practices, safety measures in place and complaint and redress systems. Member States should disseminate best practices and maintain adverse events reporting and learning systems allowing them to develop efficient solutions and interventions. Information and communication technology tools, such as electronic health records or e-prescriptions, can contribute to achieving these objectives.

As far as Directive 2004/40/EC on the protection of workers from the risks related to exposure to electromagnetic fields at work is concerned, the deadline for transposing was postponed to 30 April 2012¹⁴, in order to find solutions to reported implementation problems and to amend it as appropriate. One of the issues encountered in the current Directive is that it may unduly restrict the use of Magnetic Resonance Imaging (MRI) in medicine and research. This could result in increased use of diagnostic procedures using ionizing radiation, with an unintended adverse effect on the health of patients and workers.

1.2.2. Other tools

The objective of the Health research theme¹⁵ of the Framework Programme 7 is to improve the health of European citizens and boost the competitiveness and innovative capacity of European health-related industries and businesses, while addressing global health issues. Research into medical imaging is an important part of the health theme. In general, the objectives of the supported projects are on development and refinement of imaging techniques and methodologies, rather than on improved radiation protection of patients, which can be one of the outcomes of new technology, such as detector development.

Under the second programme of Community action in the field of health (2008-13)¹⁶ it is foreseen to promote the establishment of risk assessment networks of "*radioactive threats*"

¹² Issued by the European standards bodies in this area, CEN or CENELEC. Latest list of harmonized standards – OJ C 293, 2 December 2009

¹³ Council Recommendation of 9 June 2009 on patient safety, including the prevention and control of healthcare associated infections, O.J. C151 of 3 July 2009

¹⁴ by Directive 2008/46/EC amending Directive 2004/40/EC on minimum health and safety requirements regarding the exposure of workers to the risks arising from physical agents (electromagnetic fields)

¹⁵ http://cordis.europa.eu/fp7/health/home_en.html

¹⁶ Decision No 1350/2007/Ec of the European Parliament and of the Council of 23 October 2007 establishing a second programme of Community action in the field of health (2008-13), O.J. L 301 of 20 November 2007

and risks in the EU. The aim is to develop risk assessment capacity in the health field for "*radioactive threats*".

The so-called "*exploratory process on the future of the medical devices sector*" was put in place during the second half of 2009. The objective of the process was to establish an overview of public health and industrial challenges, to identify current dynamics of the medical devices sector and to highlight key topics of interest at the European level. The initiative provided patients, consumers, healthcare professionals, insurers and medical devices industry with an opportunity for the first time at EU level to share their views on existing challenges. One major issue identified was the need to promote innovation for the benefit of patients, healthcare professionals, industry and society, and in particular to reduce barriers to interaction and involvement of all stakeholders. A particular emphasis was put on the need to ensure a close cooperation between industry, healthcare professionals and users to better adapt research and innovation to the societal needs. The appropriate follow-up is being considered.

2. MAIN PROVISIONS OF THE EXISTING REGULATORY FRAMEWORK FOR MEDICAL EXPOSURES (DIRECTIVE 97/43/EURATOM)

2.1. Justification provisions of Medical Exposure Directive (Article 3)

According to the MED the medical exposure shall show a sufficient net benefit, weighing the total potential diagnostic or therapeutic benefits it produces against the individual detriment that the exposure might cause, taking into account the available alternative techniques involving no or less exposure to ionizing radiation. The justification shall be done on two levels: all new types of practices shall be justified in advance before being generally adopted, subject to review whenever new important evidence about their efficacy or consequences is acquired; and all individual procedures shall be justified in advance taking into account the specific objectives of the exposure and the characteristics of the individual patient.

The Medical Exposure Directive does not give much specificity on how the general justification of medical exposure practices shall be done. Yet, there are several relevant requirements specifying that: the Member States shall take appropriate steps to avoid unnecessary proliferation of radiological equipment; fluoroscopy examinations without an image intensification or equivalent techniques are not justified; fluoroscopic examinations without devices to control the dose rate shall be limited to justified circumstances; and that new radiodiagnostic equipment shall have, where practicable, a device informing the practitioner of the quantity of radiation produced during the procedure.

On the other hand, the Directive specifies several practical requirements aiming at avoiding unnecessary individual exposures including that:

- The prescriber and the radiological practitioner shall be involved as specified by Member States in the justification process at the appropriate level and, in particular, they shall seek previous diagnostic information or medical records and consider them to avoid unnecessary exposure.
- The Member States shall ensure that recommendations concerning referral criteria for medical exposure, including radiation doses, are available to the prescribers of medical exposure.
- Any medical exposure shall be effected under the clinical responsibility of a practitioner, the "clinical responsibility" including justification of the procedure.
- Clinical audits shall be carried out in accordance with national procedures.

2.2. Optimization provisions of Medical Exposure Directive (Article 4)

Medical Exposure Directive requires that the radiation doses from medical procedures shall be kept as low as reasonably achievable consistent with obtaining the required diagnostic information or therapeutic outcome, taking into account economic and social factors. The optimization process shall include the selection of equipment, the consistent production of adequate diagnostic information or therapeutic outcome as well as the practical aspects, quality assurance including quality control and the assessment and evaluation of patient doses or administered activities.

On more practical level, the Directive provides for optimization of the medical radiation procedures by: establishment and use of diagnostic reference levels; establishment of written

protocols for every type of standard radiological practice for each piece of equipment; equipment being subject to appropriate radiation protection surveillance, quality assurance, acceptance and in-service testing and dose-measuring devices requirements; appropriate involvement of a medical physics expert in the planning and conduct of the procedure; provision of adequate theoretical and practical training of the involved staff, including the radiological practitioner, the medical physicist and the technical staff physically conducting the procedure. All these requirements shall be subject to special attention when children are medically exposed, when the radiological techniques is used in a health screening programme or the technique used involves high doses to the patient, such as interventional radiology, CT or radiotherapy.

2.3. Other important provisions of Medical Exposure Directive (Articles 11, 12 and 13)

The Medical Exposure Directive requires from Member States to ensure that all reasonable steps to reduce the probability and the magnitude of accidental or unintended doses of patients from radiological practices are taken. Member States shall also ensure that distribution of individual dose estimates from medical exposure is determined for the population and for relevant reference groups of the population as may be deemed necessary.

Finally, the Medical Exposure Directive requires that the provisions of the Directive are enforced through a system of regulatory inspections.

3. SUPPLY OF RADIOISOTOPES FOR MEDICAL USE

3.1. Current situation with the supply and use of radioisotopes in nuclear medicine

3.1.1. Nuclear medicine

Nuclear medicine is a branch of medicine that uses radioisotopes (radionuclides) for the diagnosis and treatment of various diseases, including some of the most important and frequent ones, like cancers and cardiovascular diseases. It uses radioisotopes combined with pharmaceuticals to form radiopharmaceuticals. These radiopharmaceuticals, after administration to the patient by injection, inhalation or orally, reach and accumulate in specific organs or tissues, and can be detected non-invasively with high sensitivity. This unique ability distinguishes nuclear medicine from most other imaging modalities, by being primarily a functional and molecular imaging technique, studying and visualising molecular, cellular and physiological processes and functions, as opposed to traditional anatomical imaging such as computed tomography or most of magnetic resonance imaging. Therefore, nuclear medicine imaging procedures often identify abnormalities early in the progress of a disease – long before many medical problems become apparent with other diagnostic tests.

There are about 100 different nuclear medicine imaging procedures available today, including for the diagnosis of hyperthyroidism, cardiac stress tests to analyse heart function, bone scans for orthopaedic injuries or cancers, lung scans for embolism, and liver, gall bladder and kidney procedures to diagnose their dysfunctions. Over 10,000 hospitals worldwide use radioisotopes in medicine and a vast majority of the procedures (about 90%) are for diagnosis¹⁷.

3.1.2. Molybdenum-99/Technetium-99m in nuclear medicine

Technetium-99m (Tc-99m) is the most widely used isotope in nuclear medicine diagnostic applications, accounting for around 90% of all radioisotopes used, which corresponds to around 25-30 million examinations yearly worldwide, among which about 7 million in Europe. Tc-99m's main use is for cardiac imaging and bone scans to detect cancer, where early and reliable diagnosis is critical. Europe is the second largest consumer of Tc-99m, accounting for 22% of global market (after the United States – 44%), followed by Japan - 14%, and the rest of the world - 20%. Tc-99m demand is rising worldwide due to the ageing population of Europe and North America, and the growing use of the isotope in emerging countries. The predicted annual growth rate in "developed countries" is of about 3%. As for the expectations regarding the replacement of imaging modalities that use Tc-99m, major changes are currently not expected²⁷.

Tc-99m is a gamma emitter with a half-life of only 6 hours. Thus it allows for scanning procedures which collect data rapidly and keep total patient radiation exposures low. However, the short half life presents a problem in terms of a reliable supply chain since Mo-99/Tc-99m cannot be stockpiled. To allow a more practical arrangement, the supply of Tc-99m is provided by producing Molybdenum-99 (Mo-99), which decays into Tc-99m with a half-life of 66 hours. The parent isotope - Mo-99 is produced in a limited number of nuclear

¹⁷ Preliminary Report on Supply of Radioisotopes For Medical Use And Current Developments In Nuclear Medicine, SANCO/C/3/HW D(2009) Rev. 8, 30 October 2009

research reactors by irradiation of uranium targets. Once irradiated, the targets are shipped to specialized processing facilities where the Mo-99 is extracted from the irradiated targets by dissolving the targets and purifying the solution into a pharmaceutical-grade substance. Finally, the processed Mo-99 is shipped for the production of the technetium generators, from which Tc-99m can be eluted. The technetium generators are delivered to nuclear medicine facilities and hospitals for administration to the patient. Some other production schemes exist, but, as of today, their yield is much lower and the activity produced is too small to be of importance for the world market.

3.1.3. Molybdenum-99 global supply chain

Only seven government-owned nuclear research reactors provide about 95% of the world's Mo-99 production: the NRU reactor in Canada, the HFR reactor in The Netherlands, the BR2 reactor in Belgium, the OSIRIS reactor in France, the SAFARI reactor in South Africa, since March 2010 the MARIA reactor in Poland and since May 2010 the REZ reactor in Czech Republic. Several other smaller reactors provide local and regional supplies with no major influence on the global market.

Almost all the above-listed reactors are over 40 years old and are approaching the end of their life span. Because of this they have an increasing need for planned maintenance cycles and a growing frequency of unplanned production interruptions. As a result, global supply of radioisotopes became more fragile in recent years. Ten interruptions have occurred around the world since 1997, of which five in the last 3 years. In August 2008, the HFR reactor in The Netherlands, one of Europe's main research reactors producing Mo-99, was shutdown due to gas bubbles detected in the main cooling system. It remained shutdown until February 2009. In addition, routine maintenance shutdowns of the HFR reactor were undertaken in July and September 2009, with another major 6-month shutdown started on 19 February 2010 to repair the reactor's cooling water pipework¹⁸. In May 2009, the detection of a heavy water leak at the NRU reactor in Canada - also a major global supplier of Mo-99 (together with the NRU reactor supplies 65% of the world's Mo-99) - led to an extended shutdown, with the facility not expected to be fully operational until July 2010¹⁹. The European Association of Nuclear Medicine (EANM) showed by means of a survey amongst its members that the supply shortage that occurred in autumn 2008 seriously affected fourteen European countries (Belgium, Croatia, Czech Republic, France, Germany, Greece, Hungary, Iceland, Ireland, Lithuania, Netherlands, Slovakia, Switzerland and United Kingdom).

3.1.4. Economics of the Mo-99/Tc-99m supply chain

The supply chain of radioisotopes for medical use is characterized by the interaction of public and private actors and relies on global cooperation and partnership between a number of government and private stakeholders. The nuclear research reactors in which radioisotopes are produced are owned by governments all over the world. Private companies manufacture radiopharmaceuticals and distribute them to hospitals and other healthcare providers (including private practices); some of the hospitals, in which most of the nuclear medicine procedures are carried out, are publicly owned, some are operated by the private sector. Finally, public social security schemes, which provide reimbursements for a large number of nuclear medicine procedures, decide on the amounts they reimburse for such procedures.

¹⁸ High Flux Reactor powered down and repairs begun - NRG Press Release – 19 February 2010

¹⁹ AECL provides update on NRU activities - NRU Status Update #57 - 26 May 2010

The government-owned reactors where radioisotopes are produced were constructed in the 1950s and 1960s for a variety of research related purposes (nuclear research and material science). When Mo-99 production from those reactors was developed, it was considered as a “sideline” activity, so that reactor operators only required reimbursement of direct short-run marginal costs. The historical neglect of the broader direct and indirect costs led to prices for target irradiation that were too low to be of interest to industrial and commercial investors, at least at the level of production of raw Mo-99. This created a scenario in which, indirectly, some governments (those with medical radioisotope-producing reactors) subsidize the Tc-99m radiopharmaceuticals for their health services or those of other European and non-European countries.

In addition, historical prices have not been also sufficient to support the development of significant new investment in Mo-99 processing sector. As a consequence the limited number of Mo-99 processing facilities (2 in Europe) increases unreliability in the supply chain.

A study on the economics of the upstream and downstream Mo-99 and Tc-99m supply chain is part of the work plan of the OECD/NEA High-Level Group on Medical Radioisotopes (HLG-MR) established in May 2009. This group currently comprises 21 experts from 13 countries, the European Commission and the International Atomic Energy Agency. The group oversees and assists, where necessary, efforts of the international community to address the challenges of medical isotope supply reliability. The study on the economics is designed to provide a solid factual basis to develop recommendations on how the market might be structured and also aims to propose a possible environment that will attract sufficient investment in medical radioisotope production and associated infrastructure. Establishing conditions conducive to encouraging the necessary market-based private and/or public investment to bring forward additional, diversified sources of global and regional supply is considered essential to the development of a better functioning market. The study will also aim to provide a better understanding of the costs of supplying Mo-99 amongst end users in order to support a better functioning market.

3.2. Action undertaken by the Union in response to the latest supply crises

3.2.1. The EU Health Security Committee

As a result of the 2008 supply shortage, EU Health Ministers, at their meeting of 8-9 September 2008, called on the Commission to play an active role in the exchange of information on the situation. Ministers called for an emergency meeting of the EU Health Security Committee to be convened in order for the Committee to exchange information on the situation and discuss possible actions which could be taken to deal with the lack of medical radioisotopes. The European Commission convened an emergency audio-conference of the EU Health Security Committee on 11 September 2008. The item was further discussed in audio-conferences of the EU Health Security Committee of 30 September and 28 October as well as in a plenary meeting of the Committee of 5-6 November 2008 and 18 June 2009. The members of the EU Health Security Committee called on the European Commission to play an active part in the coordination of EU-wide actions to respond to the shortage.

3.2.2. The EU Task Force on Radiopharmaceuticals set-up by the European Medicines Agency

The European Medicines Agency (EMA), in order to further elaborate on a strategy to address the supply shortage of radiopharmaceuticals, has setup a Task Force which is composed of

representatives of the European Commission, Heads of Medicines Agencies of the EU Member States and the EMA. The Agency has produced a report, with status as of 24 October 2008, to the European Commission on the Supply Shortage of Radiopharmaceuticals²⁰. As part of this Report, the EU Task Force on Radiopharmaceuticals set-up by the EMA concluded with reference to longer-term aspects that there is a need to further explore possibilities for alternatives to radiopharmaceuticals in the EU. Following this recommendation, the Committee for Medicinal Products for Human Use (CHMP) agreed an action plan in May 2009 involving the organisation of a workshop with experts in the field of clinical radiology and nuclear medicine with a view to address the place of radiopharmaceuticals, labelled with radioisotopes produced in reactors, in clinical practice in the EU in the longer term and to shed light on the possible alternatives that are currently available and those that may become available in the future.

3.2.3. The EMA Workshop on Radiopharmaceuticals

The workshop took place in London on 4-5 February 2010 and confirmed that Tc-99m is the most commonly used radionuclide, thus a shortage in its supply can have major consequences in several areas where nuclear medicine imaging provides support in diagnosis and follow-up of treatment.

The experts participating at the Workshop concluded that Tc-99m use is increasing, in particular in neurology and cardiology, and the current use in bone imaging is still high although it is expected to decrease as other alternatives become available. Some other nuclear medicine imaging techniques which do not involve Tc-99m could be used in the future, including positron emission tomography (PET²¹), although it is noted that PET is currently highly dedicated mostly for oncology and partly for neurology but difficult for cardiology due to patient load and the lack of currently approved radiopharmaceuticals for myocardial perfusion. Considering the restraints in availability of PET cameras, patient management, approved indications of use, availability of PET radiopharmaceuticals and long time scales from research and development to the clinics, and the cost and trained staff implications of the single photon (SPECT²²) to positron emission computed tomography switch, other alternatives need to be considered at short term in case of Tc-99m shortage. Options include but are not limited to thallium (Tl-201) chloride for cardiology or gallium (Ga-67) citrate for infections, but these are associated with increased radiation dose and cost, and decreased image quality. Reducing the activity of Tc-99m needed per patient, in particular by favouring the use of newer software or new hardware with more sensitive detectors (in development) could also be considered.

For various indications there are currently no identified alternatives to the use of technetium without encompassing a risk on patient management. Tc-99m seems to be essential for paediatric scintigraphies, sentinel lymph node scintigraphy and intraoperative detection for

²⁰ Report to the European Commission on the Supply Shortage of Radiopharmaceuticals (status as of 24 October 2008), EMEA/51183/2009

²¹ PET (positron emission tomography) is a nuclear medicine imaging technique, and as such produces images of functional and molecular processes in the body. The system detects pairs of gamma rays emitted indirectly by a positron-emitting radionuclide administered to the body. Two- or three-dimensional images of radionuclide concentration within the body are reconstructed by computer analysis techniques.

²² SPECT (single photon emission computed tomography) is, like PET, a nuclear medicine imaging technique. But it uses gamma-emitting radionuclides and a gamma camera, like the more conventional nuclear medicine planar imaging. However, it is also able to produce three-dimensional information.

cancer treatment, parathyroid pre- and intra-operative detection, lung scintigraphy, pre-surgical localisation of epileptogenic foci in pharmaco-resistant epilepsy, and bone imaging for better indication of surgery in osteoid osteoma.

3.2.4. The EC Preliminary Report on Supply of Radioisotopes for Medical Use and Current Developments in Nuclear Medicine

Following deliberations and discussions at political and technical level and, against the background of the fragility in supply of radioisotopes for medical use around the world, the European Commission established an ad hoc inter-service group on the issue at the beginning of 2009 which has since produced a Preliminary Report on Supply of Radioisotopes for Medical Use and Current Developments in Nuclear Medicine²³. The report includes, in addition to description of current uses of radioisotopes, supply situation and available production capacities, the information about possible future initiatives regarding nuclear reactor capacities, radiopharmaceuticals and nuclear medicine, both at EU and international level. The conclusions of the report were presented to the EU Health Security Committee in June 2009 and noted by the EU Health Ministers in July 2009.

3.2.5. The Council Conclusions on the Security of Supply of Radioisotopes

On 4 November 2009 the European Commission presented its Report to the Council of the European Union. On that basis and noting that it is an appropriate time to react to the Report and give guidance for future work in addressing the continuing tight situation in the market for supply of radioisotopes, the Swedish Presidency of the Council prepared draft Council Conclusions on the Security of Supply of Radioisotopes for Medical Use. Following several rounds of examinations, on 2 December 2009 the Atomic Questions Group reached agreement on the text, which was finally adopted at the Council meeting held on 15 December 2009²⁴.

3.2.6. The EC Meeting on the Security of Supply of Medical Radioisotopes in EU Member States

In the Council Conclusions, the Commission was invited to investigate with relevant stakeholders different possible short-, medium- and long-term solutions to secure the supply of radioisotopes for medical use in the European Union, taking account of production facility projects in Member States, of technical developments and of predictions of future demand of radioisotopes in medical applications.

In response to this invitation of the Council, the Directorate-General for Energy hosted a Meeting on the Security of Supply of Medical Radioisotopes in EU Member States in Luxembourg on 4–5 May 2010, aimed at providing a forum to exchange information on possible medium-term solutions and on details of the most promising reactor opportunities for securing Mo-99 production in the long term. About 50 participants from 20 Member States attended the meeting, including the main stakeholders (reactor operators, Mo-99 processors and Mo-99/Tc-99m generator producers), the representatives from international organizations and professional associations (OECD/NEA HLG-MR, AIPES and EANM).

²³ Preliminary Report on Supply of Radioisotopes For Medical Use And Current Developments In Nuclear Medicine, SANCO/C/3/HW D(2009) Rev. 8, 30 October 2009

²⁴ Council Conclusions on the Security of Supply of Radioisotopes for Medical Use, 2986th Agriculture and Fisheries Council meeting, Brussels, 15 December 2009

- The participants of the meeting agreed that use of Tc-99m is increasing by about 3%/year in "developed countries" and that within nuclear medicine techniques, Tc-99m will remain an important isotope.
- It was highlighted that currently only EU can supply its full own Mo-99/Tc-99m needs (of course when reactors are in operation), that is why the European production network is unique.
- They agreed that there is no sufficient incentive for existing research reactors to produce Mo-99 and for new ones to be constructed with the current economic structure of the Mo-99/Tc-99m supply chain. Therefore a study on the economics of the upstream and downstream Mo-99 and Tc-99m supply is essential to identify a financial model to support the infrastructure in an economically sustainable manner and to recognise the global nature of the supply chain. Such study is part of the work plan of the NEA Secretariat of the HLG-MR and will be published in the second half of 2010.
- The participants agreed that new multi-purpose research reactors are the lowest-risk path to new Mo-99/Tc-99m production capacity, as for dedicated isotope facilities the ongoing revenues from isotope sales would be insufficient to cover the ongoing operating expenses.
- The need for harmonized radioisotope transport arrangements and uranium target design was highlighted together with the need for co-operative work to enable the future conversion to LEU targets in an efficient, timely and sustainable way.
- A need for increased efficiency of Tc-99m use was addressed by the participants (timely delivery and optimization of the use of generators along the week, etc.).
- It was agreed that alternative Mo-99 production technologies should be investigated but this is research and development over a long timescale, if it works at all, and would only solve one or few isotopes needs at a time. Indeed, reactors also produce many medical radioisotopes other than Tc-99m, in particular therapeutic ones, even though currently needed in lower quantities.
- A Position Paper by CEA, NRG, SCK•CEN and TUM²⁵ on a Reference Scenario for sustainable Mo-99 production in Europe, presented at the meeting was welcomed by the participants. In the position paper, the major European research reactor operators who are already producing, or are in a position to produce in the next few years, Mo-99 on a large scale proposed to work in an alliance to increase the future security of supply of medical isotopes by:
 - further strengthening the existing European infrastructure network approach that is supported by the position of European Research Reactors as described in the Strategic Research Agenda of the Sustainable Nuclear Energy Technology Platform,
 - working to a jointly endorsed set of common principles,
 - ensuring recovery of the investment costs of new and existing infrastructure,

²⁵

CEA - French Atomic Energy and Alternative Energies Commission (France)
 NRG - Nuclear Research & Consultancy Group (The Netherlands)
 SCK•CEN - Belgian Nuclear Research Centre (Belgium)
 TUM - University of Technology, Munich (Germany)

- ensuring availability of “on call spare capacity” and charging for its availability.
- As presented at the meeting the Reference Scenario would:
 - add a significant level of additional Tc-99m supply in Europe starting from 2014,
 - increase and strengthen the existing European supply network,
 - provide appropriate back-up capacity increasing the security of supply,
 - have sufficient capacity to back-up supply elsewhere in the world.
- According to this paper the facilities able to produce Mo-99 at the significant levels required for the medium-term European needs must be located in Europe. A possible European irradiation network for Mo-99 production should include the existing facilities still operating in the medium term:
 - BR2 (Mol, Belgium) an existing Multi-purpose Research Reactor operated by SCK•CEN (maximum capacity: >100% of European needs when operating. Operates 140 days per year; in 2010 the production capacity of BR2 has been increased by about 50%, by addition of one irradiation cycle, and by increasing the number of devices), expected to leave service by 2022 provided that the new MYRRHA facility is in operation,
 - HFR (Petten, The Netherlands) an existing Multi-purpose Research Reactor owned by the European Commission and operated by NRG, expected to leave service by 2018 provided PALLAS is in operation (maximum capacity: >100% of European needs when operating. Operates 280 days per year),
 - OSIRIS (Saclay, France) an existing Multi-purpose Research Reactor operated by the CEA (maximum capacity: ~ 25 % of European needs when operating. Operates 180 days per year), expected to leave service in 2015,
 - MARIA (Swierk, Poland) an existing Multi-purpose Research Reactor operated by POLATOM, who has started production in February 2010 (maximum capacity: ~ 10 % of European needs when operating).

And new reactors, subject to appropriate funding being available in due time:

- FRM II (Munich, Germany) a new Research Reactor operated by TUM since 2005, able to irradiate uranium targets from 2014 (maximum capacity: 50% of European needs when operating. Operates 240 days per year),
- JHR (Cadache, France) a new Materials Testing Reactor under construction to be operated by CEA, start of operation foreseen 2015 (present planned capacity: 25% of European needs; could be extended up to 50% of European needs when operating. Planned operation 220 days per year),
- PALLAS (Petten or Zeeland, The Netherlands) a proposed Multi-purpose Research Reactor to be operated from 2017 by NRG to replace HFR (estimated capacity: >100% of the European needs when operating. Planned operation 300 days per year),
- MYRRHA (Mol, Belgium) a proposed Accelerator Driven System (ADS) scheduled to be operated by SCK•CEN from 2022 (estimated capacity: equivalent replacement of BR2's capacity. Planned operation 240 days per year).

- A minimum of 200 - 250% “peak reactor capacity” was defined as necessary for Europe to ensure continuity of production during normal scheduled reactor refuelling and maintenance shutdown periods.
- Reactor operators agreed that existing European expertise might be used in the longer term to build and operate one or perhaps two new Mo-99 processing plant(s) in a more southerly location in Europe.
- They also agreed that at this moment it doesn't appear critical to consider construction of new generator production facilities, since the 3 existing largest facilities should remain operational beyond 2015.

3.3. Further involvement of the Commission to address the shortage of supply of radioisotopes for medical use

3.3.1. European research reactors infrastructure

The Sustainable Nuclear Energy Technology Platform (SNETP)²⁶ promotes research, development and demonstration in the area of nuclear systems and safety in line with an agreed vision and strategic research agenda (SRA), consistent with Strategic Energy Technology Plan (SET-Plan) goals. SNETP's SRA also identifies future needs regarding research infrastructures and competences, including new large flexible irradiation facilities, three of which (JHR in France, PALLAS in the Netherlands and MYRRHA in Belgium) have clear potential for radioisotope production in the future.

3.3.2. Financing mechanisms to ensure a sustainable supply of radioisotopes

3.3.2.1. Euratom loan

Article 172 of the Euratom Treaty foresees the possibility that *"loans for the financing of research or investment shall be raised on terms fixed by the Council."*

The Council has created such a facility in 1977, under which investments can be financed in Member States relating to industrial production of electricity in nuclear power stations or for industrial nuclear fuel cycle facilities. Since 1994, projects aiming at improving the safety level of nuclear power stations can also be financed in non-member States (currently Armenia, Russia and Ukraine). The maximum amount is limited to 20% of the investment. Currently, the amount available (of a total of €4 billion) is around €600 million. As Euratom loans are given at market conditions, the beneficiary benefits from the AAA credit rating of the Community to obtain best possible financing conditions. The loans are supplementary to financing arrangements with other parties.

Since an evaluation will be done soon, the possibility of extending the scope of the loans to include research reactors with envisaged production of radioisotopes could be explored. An extension of the Euratom loan could contribute, in the mid- and long-term, to guarantee sufficient output, and thus security of supply, of radioisotopes for patients in the European Union. Such a modification of the terms would be decided by the Council.

The provisions for this option are laid down in (Art. 172, 177(5) Euratom Treaty).

²⁶ Strategic Research Agenda, SNETP, May 2009, <http://www.snetp.eu>

3.3.2.2. European Investment Bank loan

The European Investment Bank (EIB) offers the possibilities of loans and guarantees. In the case of a small reactor producing radioisotopes, an individual loan of a maximum of 50% for a project of more than €25 million is possible. Again, the beneficiary would benefit from the AAA credit rating. The loan has to be paid back with interests, while a grace period for capital repayment may be granted during construction for a reactor. Hence, the production of radioisotopes has to generate a cash flow for the repayment of capital and interests. Technical assistance, if needed, could be given in addition to financial support.

3.3.2.3. Joint Undertaking

Joint Undertakings are possible for projects of *"fundamental importance to the development of the nuclear industry in the Community"* (Article 45 Euratom Treaty). If the security of supply of radioisotopes for medical use were considered of such fundamental importance, knowledge and resources could be bundled in a Joint Undertaking, consisting of

- Several private undertakings or
- Several public entities (Member States, Euratom, international organisation) or
- A public-private partnership.

Depending on this definition, a Joint Undertaking might also have the function of controlling the entire cycle of supply of radioisotopes (i.e. from irradiations of uranium "targets" via the extraction of Mo-99 to production and distribution of Tc-99m generators to end users)²⁷ as to ensure a better balance between public financing and private benefit.

3.3.3. Facilitating transport of medical isotopes

3.3.3.1. Simplification of administrative procedures for the trans-border transport of medical isotopes

Improvements on the side of research reactor production alone are not sufficient to assure a global supply security of medical radioisotopes. The transport of such radioactive materials is also vital. 2.5 million packages containing radioactive material are estimated to be shipped annually across the European Union, which represents about 2% of all dangerous goods packages. Most of these packages (almost 90%) contain relatively small quantities of radioactive material for medical purposes, including radioisotopes.

The currently existing comprehensive and stringent transport regulatory framework has proven to be effective in minimising the radiological impact for normal and accidental conditions of transport. However, the national deviations and disparities in the regulatory requirements and practices, which often appear to be minor, can have a major impact on trans-boundary transport of radioactive material in terms of the extra effort, time and (technical/financial) resources required by transport operators to comply with the specific national duties and requirements. Consequently, these can represent a major regulatory burden for shippers and carriers involved in intra-community and international radioactive material

²⁷ Hence, there would be a parallelism to the function of the Euratom Supply Agency (ESA) as owner and potentially "clearing house" of ores/source materials/special fissile materials (under chapter 6 of the Euratom Treaty), which was also considered of fundamental importance for the supply of materials

transport operations. These also increase the potential for non-compliances and shipment denials.

Following a three-year preparation period during which the Commission with the help of independent experts looked into the Community legislation on the transport of radioactive materials, the health and safety aspects related to it and the implementation of Community legislations, the Commission is currently examining the possibility of a new Council regulation establishing a Community system for registration of carriers of radioactive material, with the intention to harmonise and simplify administrative procedures while ensuring accessibility and transparency of this activity.

The new Council regulation does not specifically address the transport of medical radioisotopes but covers it. The main reason for this Regulation is, on one side, to try to ease the operation of the carriers by requesting one unique notification/authorisation of carriers for their operation on the whole territory of the EU. On the other side, the Regulation will provide the Competent Authorities (for the Radiation Protection aspects) with a global and exhaustive vision of the transport of radioactive materials on their national territory.

The new proposal will not solve all issues related to the Transport of Radioactive Materials but will simplify it: carriers will be required to register once into an electronic notification system and there provide the information on the nature of their transport activity in the EU. On this basis the national Competent Authority of the carrier will deliver, or not, the authorisation, valid for a period of five years and for all countries where the carrier declared operation. Procedures for the control and monitoring of the respect of rules for transport and radiation protection will continue to be applied nationally.

3.3.3.2. European Regional network on Denials of Shipment of Radioactive Material

Delays and denials of shipments of radioactive material, even if consignments are prepared fully in compliance with the regulations, have been identified by the IAEA as a cause of concern. They can result in additional risk and cost, economic hardship and at worst consumers being denied products which include radioactive material.

A Regional Workshop on Denials of Shipment of Radioactive Material for the European Region was held in Luxembourg from 17-19 June 2009. The Workshop was organised by the IAEA in cooperation with the European Commission.

The purpose of this workshop was to raise awareness of all parties concerned, i.e. suppliers, recipients, regulators, carriers/consignors and international organizations of the problems relating to denials of shipment of radioactive material with a view to determining effective measures to prevent or reduce the instances of denials in the countries of these broad geographical areas.

One of the outputs of the event was the establishment of a European regional network with a specific action plan, involving the parties concerned, and aimed at adopting accepted approaches to solving this problem.

4. ROLE AND ACTIVITIES OF INTERNATIONAL ORGANIZATIONS IN THE FIELD OF MEDICAL APPLICATIONS OF IONIZING RADIATION AND IN THE FIELD OF THE SUPPLY OF MEDICAL RADIOISOTOPES - STATEMENTS PROVIDED BY IAEA, ICRP, NEA, UNSCEAR AND WHO

INTERNATIONAL ATOMIC ENERGY AGENCY
(IAEA)

Role of IAEA in the medical application of ionizing radiation

Technology

As stated in Article II of its Statute the IAEA provides, under the technology pillar, various services to its Member States (MS) to *'accelerate and enlarge the contribution of atomic energy to peace, health and prosperity throughout the world'*. In the medical application the IAEA provides assistance to MS **in radiation medicine and on radioisotope production**.

The IAEA's activities and services to MS **in radiation medicine** involve policy dialogues, evaluation of needs assessment, technical advice, education and training, coordinated research projects, peer reviews, provision of equipment, technical publications, databases, networking and public information. Three main areas of radiation medicine in focus are: nuclear medicine, diagnostic radiology and radiation oncology.

Nuclear medicine imaging procedures with unsealed radioactive sources have become essential in managing the two major groups of non-infectious diseases, cardiovascular disease and cancer in IAEA Member States. The IAEA helps establish new nuclear medicine facilities, encourages their integration with diagnostic radiology procedures and facilitates appropriate human resources capacity building.

In diagnostic radiology, several documents have been written by the IAEA to support the quality and sustainability of mammography services with continued work also in digital mammography and computerised tomography. It is also foreseen to provide advice and expertise for the radiological diagnosis of medical conditions, including cardiovascular disease and cancer in Member States. The emerging use of tele-radiology in developing Member States is also under active investigation, in collaboration with WHO.

In radiation oncology, the IAEA works with a variety of stakeholders, including agencies within the United Nations, governments, hospitals, and research institutes to address the shortage of cancer treatment resources in Member States as documented in the IAEA directory of radiotherapy centres, DIRAC. The IAEA also promotes research and clinical applications of radiation in repairing tissue damage. Many new physical, biological and pharmaceutical tools are tested in IAEA clinical trials, through coordinated research projects, before they are introduced as improved standard treatments.

The Programme of Action for Cancer Therapy has been established to introduce and improve access to radiation cancer treatment in low income countries in cooperation with national programmes for cancer control and in collaboration with WHO and other NGOs.

The IAEA supports Member States with technical guidance for implementing and reviewing QA programmes at hospitals. The IAEA has published dosimetry protocols, which are widely used worldwide. Traceable dosimetry calibration services are provided through the IAEA/WHO Network of Secondary Standards Dosimetry Laboratories (SSDLs). Independent

dosimetry audits and comprehensive clinical audits are offered by the IAEA to radiation medicine facilities in Member States. In particular, the IAEA/WHO postal dose audit service for radiotherapy dosimetry has been in operation for over 40 years and checked radiotherapy beam calibrations in hospitals in 120 countries worldwide. Comprehensive clinical audits are provided for Member States through Quality Assurance Team for Radiation Oncology (QUATRO), Quality Assurance in Nuclear Medicine (QUANUM) and Quality Assurance Audit in Diagnostic Radiology for Improvement and Learning (QUAADRIL).

Well qualified staff is vital for safe and effective use of radiation in medicine. The IAEA has published standardized syllabi for education and training of health professionals working in radiation medicine and supports continuing education through training courses and workshops.

In the area of **radioisotopes production** the IAEA implements coordinated research projects, organises topical review meetings, compiles technical documents and updates, and provides direct assistance to MS through national and regional projects under technical cooperation programme; further, it extends cooperation support to relevant international events/meetings dealing with medical isotopes and radiopharmaceuticals. The IAEA activities related to medical isotopes and their products can be summarized as follows:

1. Capacity building and strengthening practices in production and quality control of radioisotopes and radiopharmaceuticals: Responding to MS requirements, mainly through topical meetings, technical knowledge dissemination and mostly under TC projects;
2. Fostering development of products identified to be suitable for wider production and/or distribution so as to enhance their availability and utilisation: Reactor-produced lutetium-177 & its products and generator-produced yttrium-90 and its products that can be made in several centres;
3. Facilitating adoption of PET tracers and radionuclide therapy in support of cancer management: Coordinate evaluation and deployment of products: (i) specific fluorine-18 tracers (beyond fluorodeoxyglucose, FDG) for efficacious diagnosis; (ii) Lu-177 phosphonate for metastatic bone pain palliation; (iii) Y-90 or Lu-177 peptide conjugates for treating neuroendocrine tumours;
4. Supporting measures in addressing shortages of Mo-99 supplies and related aspects of research reactor functions: i) Identifying and encouraging reactors with suitable features for Mo-99 production and facilitating cooperative efforts for regional production and supplies; ii) Assistance to adopting LEU-based production technology for Mo-99 production as well as alternate routes for Mo-99 or Tc-99m production. Iii) Contribution to and cooperation with other international initiatives, e.g. NEA instituted High Level Group on Medical Radioisotopes (HLG-MR);
5. Dissemination of technical know-how, best practices and guidelines, on medical isotopes and radiopharmaceuticals, relating to infrastructural facilities and operational processes involved;
6. Education and training of radiopharmacists and technologists; networking of researchers, end users and other stakeholders; providing appropriate forum and facilitating international cooperation and sustainable collaboration.

Safety

All IAEA activities under the pillar of safety have the ultimate goal to enhance the safety and protection of people and the environment. One of the IAEA's functions is described in its Statute as: *"to establish or adopt... standards of safety for protection of health and minimization of danger to life and property ... and to provide for the application of these ..."*.

Concerning the safe use of ionizing radiation the IAEA is undertaking various activities according to its mandate that can be summarized as follows, and which are essential for the global improvement of safety in the medical field:

1. Building the appropriate safety infrastructure

It supports Member States in the establishment and strengthening of:

- A legal and regulatory framework (laws, regulations and guides, well established, independent and competent regulatory body) that sets out clear safety requirements for workers, patients and public protection, for control of radioactive sources from their production or import to their disposal or export;
- A National strategy and a responsible Agency for ensuring the protection of patients and safer use of radiation in diagnostic, interventional and therapeutic medical procedures;
- A National strategy and a responsible Agency for the management of radioactive waste;
- National and international transport regulations (incompatible regulations between states and transport modes would prevent global trade).
- Relevant technical services in radiation safety (dosimetry, calibration of detection equipments, education and training).

2. Capacity building and networking for health professionals

Direct capacity building for the safe use of radiation in medical applications for cancer diagnosis and treatment in Member States is provided through:

- Education and training in radiation medical safety for health professionals in cooperation with WHO, including the development of guidance and training material;
- Knowledge exchange through IAEA web site on radiation protection of patients for health professionals (<http://rpop.iaea.org>);
- Direct technical assistance to Member States, such as training, missions, advice and provision of tools, as well as appraisals;
- Development of educational safety reporting systems for prevention of unintended exposures in radiological procedures and radiotherapy;
- Working towards prevention of unnecessary medical exposures by strengthening the justification process of individual medical exposures such as by International Campaigns to increase awareness.

The International Action Plan for the Radiation Protection of Patients, established in 2002 with a network of international organizations, professional bodies and experts in its Steering Panel, ensures the effective implementation of capacity building measures for the safe, optimized and justified use of ionizing radiation in medical applications. Capacity building is also provided at a broader level, for all stakeholders involved in the safety of radiation medicine:

- Education and training for radiation protection officers and regulators;
- Promotion and support of all networking activities and international cooperation (forums of regulators, steering committee on denial of shipment, networks for optimization of workers exposure in medical activities, ...);
- Promotion of international relevant undertakings: joint convention for proper management of radioactive waste and disused sources, code of conduct on the safety and security of radioactive sources, to ensure cradle to grave management, including

- import/export controls;
- Promotion and support of regional and international workshops to alleviate problems shipping radioactive material, to set strategies for waste management.

INTERNATIONAL COMMISSION ON RADIOLOGICAL PROTECTION **(ICRP)**

The Role and Activities of ICRP in the Area of Medical Applications of Ionizing Radiation and in the Field of the Supply of Medical Radioisotopes

As an observer to the Inter-Agency Committee on Radiation Safety (IACRS), the International Commission on Radiological Protection (ICRP) was asked by the European Commission to describe its role and activities in the area of medical applications of ionizing radiation and in the field of the supply of medical radioisotopes. As an observer, ICRP contributes to and supports the work of IACRS, but does not specifically endorse any reports or statements of IACRS.

ICRP, established in 1928 at the second International Congress on Radiology, is an independent, international organization that advances for the public benefit the science of radiological protection, in particular by providing recommendations and guidance on all aspects of protection against ionizing radiation. The primary aim of these recommendations is to contribute to an appropriate level of protection for people and the environment without unduly limiting the desirable human activities that may be associated with radiation exposure.

Thus the scope of ICRP's mandate includes, inter alia, radiological protection issues related to medical radioisotopes and more broadly the use of ionizing radiation in medicine, but does not include any role related to the supply of medical radioisotopes.

In preparing its recommendations, ICRP considers the fundamental principles and quantitative bases upon which appropriate radiological protection measures can be established, while leaving to the various national protection bodies the responsibility of formulating the specific advice, codes of practice, or regulations that are best suited to the needs of their individual countries.

ICRP offers its recommendations to regulatory and advisory agencies and provides advice intended to be of help to management and professional staff with responsibilities for radiological protection. Legislation in most countries adheres very closely to ICRP recommendations. In addition, the International Atomic Energy Agency (IAEA) International Basic Safety Standards for Protection against Ionizing Radiation and for the Safety of Radiation Sources (commonly referred to as "the BSS") is based heavily on ICRP recommendations, and the International Labour Organisation (ILO) Convention 115, Radiation Protection Convention, General Observation 1992, refers specifically to the recommendations of ICRP. Thus, ICRP recommendations form the basis of radiological protection standards, guidance, regulations, programmes, and practices worldwide.

ICRP is comprised of a Main Commission, a Scientific Secretariat, and five standing Committees on: Radiation effects, Doses from radiation exposure, Protection in medicine, the Application of ICRP recommendations, and Protection of the environment. In addition, ICRP uses Task Groups comprised of Committee members and other experts relevant to the subject at hand. All told, ICRP membership includes about 100 eminent scientists and policy makers in all areas of radiological protection from more than twenty-five countries.

ICRP Committee 3 on Protection in Medicine currently has 16 members, as well as observers from WHO and IEC, and is concerned with protection of persons and unborn children when ionizing radiation is used for medical diagnosis, therapy, or biomedical research, and also with the assessment of medical consequences of accidental exposures.

In recent years Committee 3 has produced a number of relevant ICRP publications, distributed through the Annals of the ICRP, including: Radiation Protection in Medicine; Radiation Dose to Patients from Radiopharmaceuticals; Managing Patient Dose in Multi-Detector Computed Tomography; Radiation safety aspects of brachytherapy for prostate cancer using permanently implanted sources; Prevention of high-dose-rate brachytherapy accidents; Release of Patients after Therapy with Unsealed Radionuclides; Managing patient dose in digital radiology, Radiation and your patient – a guide for medical practitioners; Diagnostic reference levels in medical imaging – review and additional advice; Managing Patient Dose in Computed Tomography; Prevention of accidental exposures to patients undergoing radiation therapy; Avoidance of Radiation Injuries from Medical Interventional Procedures; and, Pregnancy and Medical Radiation.

In addition, Committee 3 has recently completed two ICRP publications: Preventing accidental exposures from new external beam radiation therapy technologies; and, Radiological protection education and training for medical diagnostic and interventional procedures for healthcare staff and students.

Among the ICRP publications in development or planned for the near future within the area of radiological protection in medicine are reports on: secondary cancer risk after modern radiotherapy; practical recommendations; dose to patients from radiopharmaceuticals; radiation protection for cardiologists performing fluoroscopically guided procedures; radiation protection in charged particle radiotherapy; protecting children; follow up of persons accidentally exposed; avoiding adverse radiation effects to doctors and patients in fluoroscopically guided procedures - practical guidelines; widening the use of reference levels for interventional radiology, digital radiology and new technology; and, screening with ionizing radiation in asymptomatic individuals.

ICRP is also developing advice on radiation detriment and effective dose, including the use of these quantities in medicine.

**ORGANISATION FOR ECONOMIC CO-OPERATION AND
DEVELOPMENT/NUCLEAR ENERGY AGENCY
(OECD/NEA)**

High Level Group on the Security of Supply of Medical Radioisotopes

Background

The NEA has been requested by member countries to become involved in global efforts to ensure a reliable supply of Molybdenum-99 (Mo-99) and its decay product, Technetium-99m (Tc-99m), the most widely used medical radioisotope.

Currently five reactors commissioned between 43 and 53 years ago produce 90 to 95% of the total global supply of Mo-99. Given the age of these reactors, there are issues related to their longevity and reliability, with unexpected shutdowns occurring more often. Most recently the Canadian National Research Universal Reactor (the NRU) was shutdown in May 2009 as a result of a leak in the reactor vessel and only expects to return to service at the end of July 2010. In addition, the High Flux Reactor in the Netherlands and the OSIRIS reactor in France are scheduled to be down for extended maintenance periods. Some of these reactors are expected to reach their end of life in the next six years.

NEA Involvement

At the request of the Government of Canada, the NEA hosted a workshop of international experts and stakeholders in January 2009 to identify the challenges faced in providing a reliable supply of Tc-99m and Mo-99 and measures that should be taken to ensure this supply. Over 90 participants were in attendance, with representatives from governments, universities, reactor operators, processors, generator manufacturers and distributors, industry associations, the medical community, international organizations and regulators. There was unanimous support for the establishment of a working group to carry forward the conclusions of the workshop and to identify the practical measures that should be taken.

Formation of the High Level Group on Medical Radioisotopes

The NEA Steering Committee established the High Level Group on the Security of Supply of Medical Radioisotopes (HLG-MR) in April 2009. This group is currently comprised of 20 experts from 11 countries, the European Commission and the International Atomic Energy Agency, and is being funded by its members through voluntary contributions. The group oversees and assists, where necessary, efforts of the international community to address the challenges of medical isotope supply reliability. The NEA secretariat supports the group and brings its expertise to the issue.

The main objective of the HLG-MR is to strengthen the reliability of Mo-99/Tc-99m supply in the short, medium and long term. In order to reach this objective the group has been reviewing the Mo-99 supply chain, working to identify the key areas of vulnerability, the issues that need to be addressed and the mechanisms that could be used to address those issues. In the process of its work, the group acknowledges the common goal of converting to low enriched uranium (LEU) targets and fuel.

The HLG-MR is aware that there are a number of other on-going forums related to medical isotope supply reliability and is ensuring that efforts are not duplicated. Bringing the

international community together to discuss, share and learn, and applying NEA expertise on nuclear issues and economic studies, represent important contributions to the current global effort.

Meetings of the HLG-MR

At the first meeting on 17-18 June 2009, the first instalment of a rolling action plan was agreed upon. The plan included undertaking an economic analysis of the supply chain, increasing useful and regular communications to users about Mo-99 and Tc-99m supply availability, developing protocols to inform stakeholders of unanticipated events, and coordinating reactor schedules. The action plan also included assessing options to increase short-, medium- and long-term production. These options include demand side management (e.g., promoting efficient patient scheduling, using alternative procedures) and producing Mo-99 from alternative reactors or technologies. In terms of bringing new supply to market, the action plan included work to identify regulatory issues, especially those related to the transportation of Mo-99 and Tc-99m, and measures to address these issues

On 14-15 December 2009, the second meeting of the HLG-MR occurred with invited representatives of the nuclear regulation community, the medical isotope industry and the nuclear medicine community. Participants welcomed the positive actions that have been taken to date, such as the progress on the economic study, the development of communication protocols and the coordination and communication of reactor schedules. Participants agreed to a list of actions to further improve the management of the current shortage and to work to increasing reliable supply - the second instalment of the rolling action plan. This list included developing and implementing communication protocols; sharing guidelines with the global health community on the efficient use of available supplies of Mo-99 and Tc-99m; and examining opportunities for securing longer-term medical radioisotope supply

In addition, the HLG-MR will continue its work on examining the economics of the Mo-99 supply chain, regulatory impacts, transport difficulties and opportunities for securing Mo-99 production. The Group will start work to assess issues related to processing capacity and future Tc-99m demand.

Economic Study

As part of the work plan, the NEA Secretariat is undertaking a study on the economics of the upstream Mo-99 and Tc-99m supply chain, given the possibility of a market failure in the supply chain whereby the economic structure does not provide sufficient incentive for current reactors to produce Mo-99 or for additional production reactors to be constructed. The study, expected to be completed in mid-2010, will develop a solid factual basis of the economics of the supply chain with the goal of providing recommendations to governments on how to create a sustainable economic environment that would encourage the investments needed to ensure reliable medical isotope supplies.

Future Work

The work of the HLG is being progressed through the rolling action plan. Two reports are being prepared: the economic study and a mid-term diagnostic report. The latter will summarise the actions of the HLG-MR and Mo-99 stakeholders and will include information about the Mo-99 situation, the issues affecting its reliable supply, and actions needed to address these issues.

The HLG-MR will hold its next meeting in June 2010, again inviting supply chain stakeholders to share their perspectives. The HLG-MR will continue with its efforts to address the issues that negatively affect security of Mo-99 supply and will produce a final report in mid-2011.

UNITED NATIONS SCIENTIFIC COMMITTEE
ON THE EFFECTS OF ATOMIC RADIATION
(UNSCEAR)

Role

1. The United Nations General Assembly in its resolution 913(X) of 3 December 1955 established a Scientific Committee to compile and evaluate information on the global and regional levels and trends of exposure to ionizing radiation from all sources (including from medical applications and the supply of radioisotopes for nuclear medicine), and on the health effects of exposure.
2. The Committee therefore acts as the focal point for systematic assessments of the global and regional exposures to ionizing radiation used in medicine²⁸. It also identifies emerging issues and future research needs in the field. Its findings are reported to the General Assembly; and from time to time the United Nations publishes the associated detailed evaluations²⁹, which are used by governments, international organizations and the scientific community in supporting decisions related to the use of radiation in medicine. The evaluations represent the formal scientific underpinning for relevant international standards and capacity building programmes in the field of radiation protection, including of patients³⁰ and medical workers³¹. They also provide independent benchmarks and trends for evaluating development programmes, and represent an extensive knowledge base for education purposes.
3. The principal objectives of the recent assessments of medical exposure have essentially been to establish the annual frequency of medical examinations and procedures involving the use of radiation, as well as their associated doses. The data for these assessments are obtained by survey of United Nations Member States, review of the open scientific literature, and evaluation of specialized reports of national or regional institutes or organizations.
4. The Assembly designated 21 Member States of the United Nations as members³² of the Committee; their scientific representatives and delegations scrutinize syntheses of information prepared by experts engaged by the small Vienna-based secretariat. The European Commission has frequently participated in the annual UNSCEAR sessions as an observer.

Activities

5. The Committee assesses patient exposure using data collected through the UNSCEAR Survey of Medical Radiation Usage and Exposures (a questionnaire is sent to each United Nations Member State requesting information on the frequency of various procedures and associated doses — in the areas of diagnostic/interventional radiology, nuclear medicine, and radiotherapy — and numbers of associated staff and equipment). The Committee assesses occupational exposure (including for medical staff involved in diagnostic radiology, dental

²⁸ Assessments of medical exposures were issued in 1958, 1972, 1977, 1982, 1988, 1993, 2000, and 2008

²⁹ Available on <http://www.unscear.org>

³⁰ International action plan for the radiological protection of patients, prepared by IAEA in consultation with WHO, PAHO, and UNSCEAR, GOV/2002/36-GC(46)/12

³¹ Action plan for occupational radiation protection, prepared by IAEA and ILO, GOV/2003/47-GC(47)/7 Annex 2

³² Argentina, Australia, Belgium, Brazil, Canada, China, Egypt, France, Germany, India, Indonesia, Japan, Mexico, Peru, Poland, Russian Federation, Slovakia, Sudan, Sweden, United Kingdom, and the United States of America

radiology, nuclear medicine, radiotherapy, and other medical uses) using data collected through the UNSCEAR Global Survey of Occupational Radiation Exposures. UNSCEAR has also synthesized information from the literature on serious accidents, including those involving medical uses of radiation.

6. The Committee's strategic objective for the period 2009–2013 is **to increase awareness and deepen understanding among decision-makers, the scientific community and civil society of radiation exposure and its health and environmental effects as a sound basis for informed decision making on radiation-related issues.**

7. Medical exposure of patients has been identified as a key thematic priority for the period. The Committee will continue its surveillance on the dramatic increased global usage, both in terms of the numbers of people exposed and the levels of exposure for new medical procedures, and identify and communicate emerging issues. The secretariat envisages the next assessment to be issued in 2013.

8. Over the intervening period, UNSCEAR is seeking to: (a) streamline the conduct of its evaluations by establishing a standing expert group to maintain surveillance on emerging issues and to regularly review new information; (b) enhance the mechanisms for data collection, analysis and dissemination; and (c) raise awareness, and improve communication of the findings to decision-makers and the public.

9. With regard to enhancing data collection, UNSCEAR intends to take account of lessons identified by the EU's DOSE DATAMED project, specifically to focus its survey on the most important medical procedures contributing to population dose. There also appears to be an opportunity to harmonize the various international mechanisms and formats for collecting data on both patient and worker exposures with a view to avoiding duplication and improving the quality of the evaluations. UNSCEAR will seek to consult with the EC on these matters as appropriate.

10. With respect to assessing the risks of radiation exposure, the Committee has regularly reviewed published clinical, epidemiological (including those derived from follow-up of people medically exposed) and radiobiological information with respect to cancer risks. It has also evaluated: the developmental effects in utero of pre-natal irradiation; risks for diseases other than cancer; radiation effects on the immune and the nervous systems; the early effects of high radiation doses; the mechanisms by which radiation effects occur, including DNA repair and mutagenesis, non-targeted effects and adaptive responses in cells and organisms; the influence of dose and dose rate on risk; and the combined effects of radiation and other agents. Currently the Committee is assessing the uncertainty associated with its radiation risk estimates.

WORLD HEALTH ORGANIZATION

(WHO)

Role and activities of the World Health Organization related to medical applications of ionizing radiation

WHO is the agency within the United Nations system with specific mandate on international public health work. A mechanism for internal collaboration between relevant WHO programs addressing radiation and human health is in place to coordinate actions, promote synergies and avoid duplication of efforts.

The WHO Department of Public Health and Environment (PHE)³³ conducts a Radiation and Environmental Health programme³⁴ which comprises a Global Initiative on Radiation Safety in Health Care Settings (GI) to mobilize the health sector towards safer use of radiation in medicine³⁵. This initiative brings together health authorities, international organizations, professional bodies, scientific societies and academic institutions in concerted action to improve the implementation of radiation safety standards in healthcare settings. The strategic approach adopted includes activities in the areas of risk assessment, risk management and risk communication:

Cooperation with UNSCEAR was strengthened within the GI to improve data collection and assist countries through capacity building and technical support to conduct national surveys on medical exposures. This collaboration with UNSCEAR includes plans towards shaping a global research agenda on health effects from medical exposures, considering a strategic research agenda on radiation risks of medical exposures early in life.

The GI is currently focusing on justification of medical exposures. An international consultancy on referral guidelines (RGs) for appropriate use of radiation imaging was held in March 2010 gathering experts from 23 international, regional and national professional societies from all WHO regions, as well as representatives from the EC and IAEA³⁶. An international collaboration was established to develop a global set of evidence-based RGs as tools for justification. Plans to facilitate the RGs implementation, monitor their use and evaluate the impact in different clinical settings were proposed³⁷. The GI advocates for the inclusion of radiation protection (RP) contents in the curricula of medical and public health schools and will promote the use of RGs as education tools for medical students and young

³³ http://www.who.int/topics/environmental_health/en/

³⁴ http://www.who.int/ionizing_radiation/en/

³⁵ http://www.who.int/ionizing_radiation/about/med_exposure/en/index.html.

³⁶ Alliance for Radiation Safety in Paediatric Imaging- Image Gently Campaign, American College of Radiologists (ACR), Argentine Society of Radiology (SAR), African Society of Radiology (ASR), Association of General Practitioners (Geneva), Canadian Association of Radiologists (CAR), Chinese Society of Radiology (CSR), European Commission (EC), European Society of Radiology (ESR), Federal Office for Radiation Protection (BfS, Germany), Hong Kong College of Radiologists (HKCR), Inter-American College of Radiologists (CIR), International Atomic Energy Agency (IAEA), International Pediatric Association (IPA), International Radiology Quality Network (IRQN), International Society of Radiology (ISR), International Society of Radiographers and Radiological Technologists (ISRRT), National Centre for Child Health and Development (NCCHD, Japan), Nuclear Safety Authority (ASN, France), Pan American Health Organization (PAHO), Royal and Australian New Zealand College of Radiologists (RANZCR), Royal College of Radiology (RCR, UK) and World Health Organization (WHO)

³⁷ More information is available at
http://www.who.int/ionizing_radiation/about/med_exposure/en/index2.html

doctors. A number of activities are being conducted in the field of radiation protection in pediatric health care (e.g. workshops, specialists seminars, training for pediatricians). A tool kit on radiation risk communication in paediatric imaging is being developed, including ethical considerations and guidance on informed consent. A workshop on radiation risk communication in pediatric imaging will be held in September 2010.

WHO is cooperating with EC, IAEA, ILO, IOMP, IFMBE, IRPA and ISRRT³⁸ in several activities/projects addressing staffing needs, in particular addressing medical physicists training and recognition and role of radiographers and radiation technologists in the implementation of radiation protection (RP) policies. A global plan of action for worker's health is being implemented by WHO between 2008-2017 to assess and manage occupational hazards including ionizing radiation, in cooperation with ILO and IAEA.

WHO conducts a patient safety programme (PSP) that promotes patient safety reporting and learning systems, including taxonomy and development of an International Classification for Patient Safety³⁹. WHO established the "Patients for Patients Safety" global network to support patient engagement⁴⁰. The Technical Manual on Radiotherapy Risk Profile⁴¹ developed by the PSP was presented during the International Conference on Modern Radiotherapy, organized by the ASN in cooperation with EC, IAEA and WHO.

The use of radiation in health care is also addressed through the Global Action Against Cancer to promote the basic components of cancer control: prevention, early detection, diagnosis and treatment, and palliative care. WHO collaborates with the IAEA in the Programme of Action for Cancer Therapy (PACT)⁴². Through the International Agency for Research on Cancer (IARC) WHO coordinates and conducts experimental and epidemiological research on the causes of cancer, including ionizing radiation.

WHO assists countries in establishing and optimizing the use of health technologies. The Department of Essential Health Technologies (EHT) conducts a program on Diagnostic Imaging and Medical Devices (DIM) aimed at making safe and reliable diagnostic imaging services available to as many as possible, and providing advice, guidance and technical support for developing and maintaining diagnostic imaging services⁴³.

The WHO Department of Essential Medicines and Pharmaceutical Policies (EMP)⁴⁴ through its Quality Assurance and Safety (QAS) program is involved in the setting of standards for essential medicines. These standards address good manufacturing practices (GMP) and good distribution practices (GDP) for pharmaceutical products, including radiopharmaceuticals. A GMP text on radiopharmaceuticals was developed in collaboration with IAEA and plans to revise and update this text are considered. WHO/EMP has collaborated with the IAEA

³⁸ EC: European Commission, IAEA: International Atomic Energy Agency, ILO: International Labour Organization, IOMP: International Organization of Medical Physics, IFMBE: International Federation of Biomedical Engineering, IRPA: International Radiation Protection Association, ISRRT: International Society of Radiographers and Radiation Technologists.

³⁹ <http://www.who.int/patientsafety/implementation/taxonomy/en/>.

⁴⁰ http://www.who.int/patientsafety/patients_for_patient/en/

⁴¹ http://www.who.int/patientsafety/activities/technical/radiotherapy_risk_profile.pdf.

⁴² <http://www.who.int/topics/cancer/en/> and

http://www.who.int/mediacentre/news/releases/2009/who_iaea_cancer_programme_20090526/en/

⁴³ http://www.who.int/diagnostic_imaging/en/index.html

⁴⁴ <http://www.who.int/medicines/about/en/index.html>

on quality control testing, and the monographs emanating from this collaboration will be included in a future publication of the International Pharmacopoeia⁴⁵.

WHO engages in international partnership when joint action in the field of radiation protection is needed. This policy is reflected in its engagement in the current BSS⁴⁶ revision process as a member of the joint BSS Secretariat and its participation in the Inter-Agency Committee for Radiation Safety (IACRS). In the field on RP in medical exposures the collaboration comprises EC, ICRP⁴⁷, ILO, IAEA, IRPA⁴⁸, NEA⁴⁹ and UNSCEAR.

⁴⁵ More information about distribution is available at:
http://whqlibdoc.who.int/trs/WHO_TRS_908.pdf#page=36
http://www.who.int/medicines/areas/quality_safety/quality_assurance/distribution/en/index.html
<http://www.who.int/medicines/publications/pharmacopoeia/overview/en/index.html>
<http://www.who.int/medicines/publications/pharmacopoeia/radiopharm/en/index.html>

⁴⁶ BSS: International Basic Safety Standards for Protection against Ionizing Radiation and for the Safety of Radiation Sources

⁴⁷ ICRP: International Commission on Radiological Protection.

⁴⁸ IRPA: International Radiation Protection Association.

⁴⁹ NEA Committee on Radiation Protection and Public Health (CRPPH), expert group on Public Health Perspective in Radiological Protection (EGPH)